

95F1968
RR



Department of Defense

**Comprehensive
Clinical Evaluation Program
for
Gulf War Veterans**

Report on 10,020 Participants

August 1995

#783

ABSTRACT

In response to veterans' concerns about potential health effects resulting from service during Operations Desert Storm/Shield, the Department of Defense (DoD) initiated the Comprehensive Clinical Evaluation Program (CCEP). To date, the CCEP has provided in-depth medical examinations to approximately 13,000 service and family members entitled to DoD health care. This descriptive case series report summarizes the diagnostic results of 10,020 participants who have finished their medical evaluations. Designed as a clinical rather than a research program, the results of the CCEP provide insight into the nature of symptoms and diagnoses in this self-selected group of individuals. In general, the demographic characteristics of CCEP participants represent a cross-section of Persian Gulf War veterans as a group. CCEP participants self-report a range of wartime occupational and environmental exposures. Symptoms and diagnoses seen in CCEP participants resemble those seen in the general population and in patients seeking primary care. Psychological, musculoskeletal, and nonspecific conditions represent the major categories of primary diagnoses, and may occur more frequently in the CCEP than in other primary care settings. Research studies with comparison groups of non-deployed Persian Gulf-era veterans will clarify whether or not these conditions may be more common among Persian Gulf War veterans. Severe disability measured in terms of lost work days does not appear to be a major characteristic of the clinical profile of CCEP participants. However, participants experiencing disabling symptoms may benefit from programs which have been established at DoD Specialized Care Centers that focus on rehabilitation, restoration of function and promotion of general well being. Finally, based on the CCEP experience to date, there exists no clinical evidence for a new syndrome or unique illness among Persian Gulf veterans. The results of the CCEP are consistent with conclusions of a National Institutes of Health Technology Assessment Workshop that "no single disease or syndrome is apparent, but rather multiple illnesses with overlapping symptoms and causes." DoD will arrange for independent researchers to have access to the CCEP data in the future.

Table of Contents

	Page
ABSTRACT.....	i
EXECUTIVE SUMMARY.....	1
INTRODUCTION.....	3
POTENTIAL HEALTH RISKS ASSOCIATED WITH PERSIAN GULF DEPLOYMENT	3
THE COMPREHENSIVE CLINICAL EVALUATION PROGRAM PROCESS.....	6
INSTITUTE OF MEDICINE.....	7
RESULTS.....	8
PROGRAM STATUS	8
DEMOGRAPHICS.....	9
UNIT OF ASSIGNMENT	10
SELF-REPORTED EXPOSURES	10
SYMPTOMS	11
DIAGNOSTIC CATEGORIES	13
SELF-REPORTED WORK DAYS LOST DUE TO ILLNESS.....	17
SATISFACTION WITH CCEP	18
DISCUSSION.....	18
EPIDEMIOLOGICAL CONSIDERATIONS.....	18
COMPARISON GROUP SELECTION	18
DEMOGRAPHICS.....	19
UNIT IDENTIFICATION CODES - SPECIFIC PARTICIPATION RATES.....	19
USE OF UNIT IDENTIFICATION CODES TO VALIDATE SELF-REPORTED EXPOSURES	20
SYMPTOMS	21
EXISTENCE OF A UNIQUE ILLNESS	23
CCEP DIAGNOSES RELATIVE TO OTHER AMBULATORY CARE STUDIES	23
PSYCHOLOGICAL CONDITIONS.....	26
ILL DEFINED SIGNS AND SYMPTOMS	28
MUSCULOSKELETAL CONDITIONS	28
ADDITIONAL DIAGNOSTIC CONSIDERATIONS.....	29
INFECTIOUS DISEASES	29
FATIGUE.....	30
SLEEP.....	30
MEMORY PROBLEMS	31
DIAGNOSES IN SPOUSES AND CHILDREN	31
REPRODUCTIVE HEALTH CONCERNS	32
DISABILITY.....	32
PATIENT SATISFACTION.....	33
ADDITIONAL RESEARCH EFFORTS	33
INDIVIDUAL AND GROUP RESPONSE TO ENVIRONMENTAL HAZARDS AS A FACTOR CONTRIBUTING TO HEALTH CONSEQUENCES AMONG CCEP PARTICIPANTS	34
CONCLUSIONS.....	35

Tables

	Page
TABLE 1. DEMOGRAPHIC VARIABLES OF CCEP PARTICIPANTS AND PERSIAN GULF WAR PARTICIPANTS	9
TABLE 2. CCEP SELF-REPORTED EXPOSURE HISTORY (N = 10,020).....	11
TABLE 3. SYMPTOM FREQUENCY FOR CCEP PARTICIPANTS (N = 10,020).....	12
TABLE 4. FREQUENCY DISTRIBUTION OF PRIMARY AND ANY DIAGNOSIS AMONG 10,020 COMPLETED CCEP EVALUATIONS (BY ICD-9-CM CATEGORY)	14
TABLE 5. FREQUENCY DISTRIBUTION OF PRIMARY AND ANY DIAGNOSIS AMONG 136 COMPLETED CCEP EVALUATIONS OF SPOUSES (BY ICD-9-CM CATEGORY).....	16
TABLE 6. FREQUENCY DISTRIBUTION OF PRIMARY DIAGNOSES AMONG 81 CHILDREN OF PERSIAN GULF WAR VETERANS IN THE CCEP.....	17
TABLE 7. PREVALENCE OF VARIOUS SYMPTOMS IN 3 COMMON SYMPTOM SYNDROMES COMPARED WITH CCEP PATIENTS	22
TABLE 8. FREQUENCY DISTRIBUTION OF PRINCIPAL DIAGNOSES IN U.S. AMBULATORY CARE SURVEY (NAMCS) AND IN THE CCEP	24
TABLE 9. PREVALENCE OF PSYCHOLOGICAL CONDITIONS IN CCEP PARTICIPANTS COMPARED TO OTHER COMMUNITY AND PRIMARY CARE COHORTS.....	26
TABLE 10. MOST COMMON PSYCHOLOGICAL CONDITIONS AMONG CCEP PARTICIPANTS, GENERAL POPULATION AND PRIMARY CARE PATIENTS.....	27

Figures

	Page
FIGURE 1. DISPOSITION OF CCEP PARTICIPANTS AS OF MAY 31, 1995.....	8
FIGURE 2. DISTRIBUTION OF PRIMARY DIAGNOSES AMONG 10,020 CCEP PARTICIPANTS....	15
FIGURE 3. COMMON SYMPTOM PREVALENCE AS REPORTED IN 3 STUDIES OF OUTPATIENT PRACTICE IN THE UNITED STATES, AS COMPARED WITH CCEP.....	21

EXECUTIVE SUMMARY

Comprehensive Clinical Evaluation Program for Gulf War Veterans: Report on 10,020 Participants

Approximately 697,000 U.S. service members deployed to the Persian Gulf in 1990/1991 for Operations Desert Shield/Desert Storm (ODS/S). The vast majority of troops returned from this large deployment healthy and remain fit for duty today. In response to Gulf War veterans' concerns about the potential health effects of service in ODS/S and to further investigate the nature of their illnesses, the Departments of Defense (DoD) and Veterans Affairs (DVA) developed similar, comprehensive clinical evaluation programs. The DoD's Comprehensive Clinical Evaluation Program (CCEP) provides an in-depth medical evaluation for DoD beneficiaries who are experiencing illnesses which may be related to their service in the Persian Gulf. Currently, the program has enrolled nearly 23,000 participants. Approximately 17,000 of these participants have requested an examination, of which over 13,000 have finished the evaluation process, and the records of 10,020 have been verified and entered into the CCEP database.

This descriptive case series report summarizes the diagnostic results of over 10,000 systematic clinical evaluations completed through the CCEP. The CCEP was designed primarily as a clinical rather than research program. Self-selection of patients, recall bias, inability to validate self-reported exposures and lack of a control group limit the relevance of CCEP findings to other Persian Gulf veterans. However, the large size of the CCEP cohort and the thoroughness of the CCEP examinations provide considerable clinical insight towards understanding the nature of these veterans' illnesses and health concerns. Ongoing and planned DoD/VA/HHS sponsored epidemiologic studies involving control/comparison populations will characterize further the health consequences of the Persian Gulf War. Based on the evaluation of 10,020 participants, our findings include:

- To date, the CCEP has identified no clinical evidence for a new or unique illness or syndrome among Persian Gulf veterans. The results of the CCEP are consistent with the conclusion of a National Institutes of Health Technology Assessment Workshop that "no single disease or syndrome is apparent, but rather multiple illnesses with overlapping symptoms and causes."
- Symptoms reported by CCEP participants are similar to those seen in patients seeking primary care based on studies of outpatient practice and of the general U.S. population. CCEP patients demonstrate a broad cross-section of diagnoses which would be expected in this large population.

- Generalized symptoms such as fatigue, joint pain, headache, and sleep disturbances are very common among CCEP participants. Published studies of patients with these types of generalized symptoms have shown that 20-75% of them lack a clear-cut or discrete physical explanation or “cause” after a thorough medical evaluation. Similarly, it is likely that some CCEP participants may also lack a discrete physical explanation for their generalized symptoms.
- The distribution of International Classification of Diseases-9th Revision, Clinical Modification (ICD-9-CM) diagnostic categories seen in CCEP participants resembles that seen in the general population and in patients seeking primary care. “Psychological,” “Signs, Symptoms, Ill-Defined Conditions,” and “Musculoskeletal & Connective Tissue” represent the major ICD-9-CM categories of primary diagnoses.
- Severe disability, measured in terms of reported lost work days, is not a major characteristic of CCEP participants. Most CCEP participants (81%) had not missed work because of illness or injury during the 90 days prior to their initial evaluation. Seven percent of CCEP participants self-reported missing more than one week of work due to illness.
- Comparisons of CCEP participants to patients in outpatient medical settings are limited because of differences in patient populations. However, preliminary conclusions are as follows:
 - * The most common psychological conditions found in CCEP participants are: tension headache; nonspecific, mild or stress-related anxiety and/or depression; posttraumatic stress disorder (PTSD). The prevalence of psychological diagnoses among CCEP participants may be higher than that observed in other patients seen in general medical practice.
 - * CCEP diagnoses include a group of well-defined conditions not classified elsewhere in the ICD-9-CM coding system (e.g. sleep apneas), generalized symptoms, abnormal laboratory tests, and nonspecific physical findings. These diagnoses which are categorized as “Signs, Symptoms and Ill-Defined Conditions” according to the ICD-9-CM coding system may be more common in the CCEP compared to patients seen in general medical practice.
 - * Musculoskeletal and connective tissue diseases (joint pain, osteoarthritis, backache) are common diagnoses seen in CCEP participants. These conditions appear to occur more frequently in the CCEP population compared to patients seen in general medical practice.
- DoD will continue to provide comprehensive quality health care to eligible Persian Gulf veterans, and will maintain an ongoing search for unique symptom/illness patterns. The Department is committed to a continuing exchange of relevant information with other government agencies and Gulf War veterans to further understand this public health issue.

Introduction

Approximately 697,000 U.S. service members deployed to the Persian Gulf in 1990/1991 for Operations Desert Shield/Desert Storm (ODS/S). Medical readiness planning and preventive medicine measures taken by the DoD contributed to U.S. military forces experiencing the lowest disease non-battle injury (DNBI) rate of any major conflict. The vast majority of soldiers, sailors, airmen, and marines returned from this large deployment healthy and remain fit for duty today. Since ODS/S, veterans seeking medical care have had a wide range of conditions that would be expected in such a large adult population. Some service members have had persistent symptoms which they believe are related to their experience in the Persian Gulf War. In response to Gulf War veterans' concerns about their health following ODS/S, the Departments of Defense (DoD) and Veterans Affairs (VA) developed similar comprehensive clinical evaluation programs. To date, the DoD has enrolled approximately 23,000 participants eligible for DoD health care in the Comprehensive Clinical Evaluation Program (CCEP).

In December, 1994, the DoD issued its preliminary status report on the first 1,000 patients to complete the CCEP. Since that report, the Department has continued an aggressive outreach effort to provide evaluation and care to veterans who are experiencing symptoms or illnesses which they feel may be related to their service in the Persian Gulf. The DoD provided an update on March 10, 1995, regarding the results of 2,076 medical evaluations accomplished through the CCEP. This report summarizes program activities through May 31, 1995, and includes the clinical findings from 10,020 patients who have completed their CCEP evaluations.

Potential Health Risks Associated With Persian Gulf Deployment

In order to better understand the potential causes of illnesses and most effective treatments for Gulf War veterans, a thorough review of the potential health risks associated with service in the Persian Gulf is necessary. These risks include: physical and psychological stress, possible reactions to prophylactic drugs and vaccines, infectious diseases, and potential exposures to environmental hazards.¹

Physical and psychological stressors were major characteristics of the Persian Gulf. The effect of both acute and chronic stress is a major etiologic consideration when evaluating Persian Gulf veterans. U.S. troops entered a bleak, physically demanding, desert environment, where they were

crowded into warehouses, storage buildings, and tents with little personal privacy and few amenities. No one knew that coalition forces eventually would win a quick war with relatively few battle casualties. Consequently, most troops did not fight a "four day war" but spent months isolated in the desert, under constant stress, concerned about their survival and their family's well-being at home, and uncertain about when they would return home.² Since the end of the war, readjustment disorders and posttraumatic stress disorder (PTSD) have been frequently reported among Persian Gulf veterans.^{3,4,5}

Although exposure to chemical warfare (CW) and biological warfare (BW) agents has been hypothesized as a possible cause of ill health among the returning veterans, both a DoD Defense Science Board Task Force and the Institute of Medicine have concluded that there is no persuasive evidence that Iraq used CW/BW weapons or that there was exposure of U.S. troops.^{6,7}

To provide protection against the lethal effects of CW nerve agents, troops were issued twenty-one 30 mg tablets of pyridostigmine bromide.⁸ Pyridostigmine bromide has been suggested as a cause of chronic illness in Gulf veterans. However, this Food and Drug Administration (FDA)-approved drug has been used since the 1950s in anesthesia and as a treatment for myasthenia gravis with no known long-term health effects. In addition, studies of this drug in low doses have not revealed any serious lasting side-effects.^{9,10,11} Nonetheless, studies to evaluate the potential health effects of pyridostigmine, both alone and in combination with other agents, are ongoing.

Vaccines which protect against anthrax and botulism also have been mentioned as possible causes of ill health. Anthrax vaccine is a FDA licensed product. Although botulinum toxoid is not available as a licensed product, FDA approved its use by DoD as an Investigational New Drug after review of available safety information. Anthrax vaccine and botulinum toxoid have been given to military and civilian personnel worldwide for several decades without any long-term adverse effects.^{7,12,13} Approximately 150,000 service members received anthrax vaccinations, while botulinum toxoid was administered to about 8,000 troops.

The surveillance and impact of infectious diseases during the Persian Gulf War have been summarized recently.¹⁴ The major reported causes of acute morbidity were generally mild cases of acute diarrhea and upper respiratory disease. There was a decided absence of expected arboviral infections, particularly sandfly fever. Infectious diseases were not a major cause of lost manpower during ODS/S.

Since the Gulf War, thirty-one cases of leishmaniasis have been diagnosed among U.S. troops consisting of nineteen cases of cutaneous and twelve cases of viscerotropic leishmaniasis.¹ The nineteen cases of cutaneous leishmaniasis exhibited characteristic skin lesions. All but one of the individuals with documented viscerotropic leishmaniasis have had characteristic, objective signs of disease, including fever, swollen lymph glands, and enlarged liver or spleen.¹⁵

Some Desert Storm troops may have been exposed to several potentially harmful environmental hazards, most notably smoke from 605 burning oil wells. The U.S. Army conducted an extensive health risk assessment (HRA) of smoke exposure which included methodology developed by the Environmental Protection Agency. The HRA determined long-term health risks to be minimal in part because of the nearly complete combustion of most chemical substances and the lofting of the smoke above ground level.^{16,17}

Other potential environmental hazards that some service members may have been exposed to include: depleted uranium munitions, microwaves, chemical-agent-resistant-coating (CARC) paint vapors, various petroleum products, pesticides, and airborne allergens and irritants.¹⁸ None of these exposures has been identified as a major cause of illness among Persian Gulf veterans, either because exposures involved small numbers of troops or because the agents are not known to cause the chronic symptoms reported by returning veterans.^{6,7,14,16}

The Comprehensive Clinical Evaluation Program Process

Because of concern for the medical problems of Persian Gulf veterans and to better understand the nature of the diverse symptoms being reported, DoD established the CCEP on June 7, 1994. The CCEP provides a systematic, in-depth, medical evaluation for all military health care beneficiaries who are experiencing illnesses which they believe may be related to Persian Gulf deployment. Spouses and children of Gulf War veterans may participate in the CCEP if they are eligible for DoD health care.

Participants enroll in the program either by contacting their local military medical treatment facility or by calling a toll free number (1-800-796-9699) which provides information to individuals requesting medical evaluations. Every military medical treatment facility (MTF) has a designated CCEP physician coordinator who is a board-certified family practitioner or internal medicine specialist.

Developed by a multidisciplinary team of DoD and VA medical specialists, the CCEP provides a two-phase, comprehensive medical evaluation. Phase I is conducted at the local MTF and consists of a history and medical examination comparable in scope and thoroughness to an evaluation conducted for an in-patient hospital admission. The medical review includes questions about family history, health, occupation, unique exposures in the Gulf War, and a structured review of symptoms. Health care providers specifically inquire about the symptoms and exposures listed on the "CCEP Provider-Administered Patient Questionnaire." The medical examination focuses on patients' symptoms and health concerns, and includes standard laboratory tests (complete blood count, urinalysis, serum chemistries) and other tests as clinically indicated. Individuals who require additional evaluation after completing the MTF-level, Phase I evaluation and appropriate consultations may be referred to one of fifteen Regional Medical Centers (RMCs) for Phase II evaluations. Phase II evaluations consist of symptom-specific examinations, additional laboratory tests, and specialty consultations according to the prescribed protocol.

The DoD has established a Specialized Care Center (SCC) at Walter Reed Army Medical Center (Eastern Region), and has planned a second center for Wilford Hall Medical Center (Western Region) to provide additional evaluation, care and rehabilitation for CCEP participants who are suffering from chronic, debilitating symptoms. An intensive 3 week evaluation and care program designed to restore participants to a maximum state of health and fitness is provided by

the SCCs. A multidisciplinary team of physicians from various specialties, behavioral health psychologists, nurses, and physical and occupational therapists comprise the staff of the SCCs. The treatment program is modeled after multidisciplinary pain centers, which have proven effective in treating patients with chronic, debilitating syndromes.

Institute of Medicine

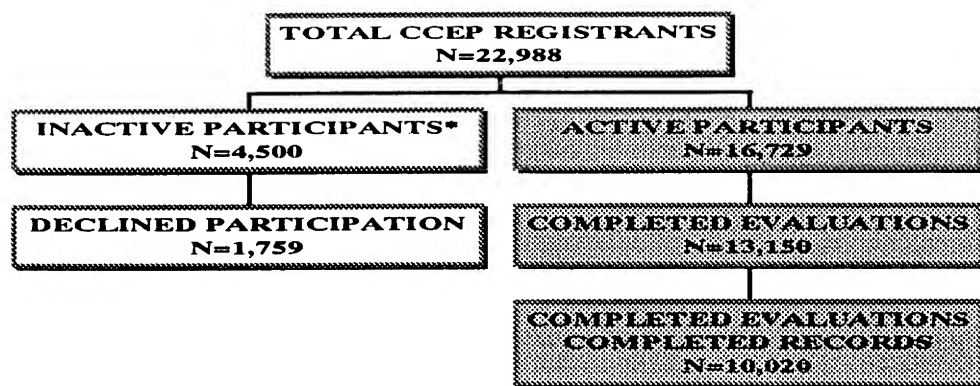
The DoD requested the Institute of Medicine (IOM) to serve as a consultant to review the CCEP. The IOM formed a panel of experts in epidemiology, occupational medicine, internal medicine, infectious diseases, psychiatry/psychology, community mental health, allergy/immunology, and other disciplines. The panel has met with the CCEP military physicians and other DoD representatives on two occasions to review both program process and results to date. The IOM initial report of December 1994 stated that the CCEP represented a thorough and systematic approach to the diagnosis of a wide spectrum of illnesses. The IOM recommended that a greater proportion of the CCEP evaluations be accomplished in Phase I to expedite the diagnostic process and facilitate continuity of care at the local level. A second IOM report is projected for the summer of 1995.

RESULTS

Program Status

Of the 16,729 participants who requested medical examinations through the CCEP, 10,020 records have been entered into the CCEP computerized database (Figure 1). MTFs send reports of finished medical evaluations to a central program management office where administrative staff and medical coders review records for completeness and accuracy of diagnostic coding before entering the data into a computerized database. Eighty-three percent (83%) of CCEP evaluations were completed at Phase I and seventeen percent (17%) at Phase II.

Figure 1. Disposition of CCEP Participants as of May 31, 1995



* Inactive Participants include those participants who wish to defer their medical evaluation until a later time.

Demographics

The demographic characteristics of 10,020 CCEP participants who have completed their evaluations are compared with the characteristics of all Gulf War veterans in Table 1. Statistically significant differences ($p < 0.05$) are noted for each of the demographic categories with the exception of Hispanic ethnicity, rank, and Air Force affiliation. Additionally, CCEP participants are two years older on average than all Persian Gulf War veterans.

Table 1. Demographic Variables of CCEP Participants and Persian Gulf War Participants

Characteristics	CCEP Participants N=9,798 ¹	Total PGW Participants N=697,000
<u>Gender(%)</u>		
Male	88	93
Female	12	7
<u>Race(%)</u>		
White	60	70
Black	30	23
Hispanic	6	5
Other	4	2
<u>Rank(%)</u>		
Enlisted	89	89
Officer	10	10
Other/No Data	1	1
<u>Branch(%)</u>		
Air Force	12	12
Army	78	50
Marine	4	15
Navy	5	23
Other/No Data	1	
<u>Status(%)</u>		
Active	82	83
Reserve/Guard	8	17
Other/No Data	10	
<u>Age (Yrs)</u>	34 ²	32 ³

¹Includes only service members.

²The average age of the CCEP participants is as of June 1995.

³ The average age of the PGW participants is as of June 1995.

Unit of Assignment

The approximately 700,000 personnel who deployed to the Persian Gulf War were assigned to military units designated by 13,448 different unit identification codes (UICs). The number of deployed personnel assigned to a single UIC varied from one person to several thousand (e.g., an aircraft carrier crew). Additionally, the Air Force used a limited number of large “administrative” UICs (for one example, one UIC had 20,978 personnel assigned). Some deployed personnel were subsequently assigned to multiple UICs throughout the theater.

Of the 10,020 CCEP participants with completed evaluations, 7,610 (76%) had UIC information available. These CCEP participants are representative of 2,725 different UICs, to which 443,898 service members (60% of the total force) were assigned. CCEP participants served in a very large number of different units, and eighty-five percent (85%) of UICs represented in the CCEP had four or fewer participants. Two hundred (200) individuals in the CCEP served in 62 different units (of 10 or more persons assigned) where CCEP participation rates were equal to or exceeded 10% of members of that UIC.

Self-Reported Exposures

The “CCEP Patient Questionnaire” asks the participants about exposures they experienced during the Persian Gulf War. This “self-reported” exposure information is dependent upon the participant’s ability to recall events. Confirmation or validation of self-reported exposures was not possible using existing data sources for a given individual’s exposures.

Table 2 summarizes the most frequently self-reported exposures, including: passive cigarette smoke (86%), diesel/other fuels (85%), pyridostigmine bromide tablets (70%), oil fire smoke (68%), and tent heater fumes (68%). Least often reported were suspected nerve gas/nerve agents (5%) and mustard/blistering agents (2%). The average number of positive exposure responses per CCEP participant was 11 of 20 potential exposures. Twenty-nine percent (29%) of the CCEP participants report they are current smokers, smoking an average of 16 cigarettes per day.

Table 2. CCEP Self-Reported Exposure History (n=10,020)

Exposures Reported By Participant	Positive Report	
	Number	%
Cigarette Smoke (Passive)	8,667	86
Diesel/Other Fuels	8,547	85
Pyridostigmine Bromide	7,020	70
Tent/Heater Fumes	6,784	68
Oil Fire Smoke	6,863	68
Personal Pesticide Use	6,400	64
Ate Non-U.S. Food	6,369	64
Had Anthrax Immunization	4,956	49
Solvent	4,508	45
Chemical Agent Resistant Coating (CARC) Paint	4,363	44
Other Paint	3,927	39
Microwaves	3,469	35
Bathed In/Drank Non-U.S. Water	3,199	32
Had Botulism Immunization	2,558	26
Taken Oral Medicine To Prevent Malaria	2,649	26
Ate Contaminated Food	2,050	20
Bathed In Contaminated Water	1,934	19
Depleted Uranium	1,415	14
Nerve Gas/Nerve Agents	501	5
Mustard Gas/Blistering Agents	234	2

Symptoms

The CCEP medical evaluation documents participants' chief health complaints and any other health complaints they may be experiencing.

Table 3 summarizes the frequency distribution of positive responses to the “Provider-Administered Symptom Questionnaire.” The most frequently reported chief complaints were: fatigue (11%), joint pain (11%), headache (8%) and memory loss (4%). Among the reported symptoms, whether a chief or associated complaint, the most common symptoms from the symptom questionnaire included: fatigue (47%), joint pain (47%), headache (39%), memory loss (33%), sleep disturbance (32%), and difficulty concentrating (27%). The average number of reported symptoms for CCEP participants was five.

Table 3. Symptom Frequency for CCEP Participants (N=10,020)

Symptoms Reported By Participants	Chief Complaint	Any Complaint
Fatigue	11%	47%
Joint Pain	11%	47%
Headache	8%	39%
Rash/Dermatitis	7%	29%
Memory Loss	4%	33%
Abdominal Pain/Gastrointestinal	2%	16%
Back Pain	2%	2%
Diarrhea	2%	18%
Dyspnea	2%	16%
Sleep Disturbance	2%	32%
Chest Complaints	1%	1%
Cough	1%	1%
Depression	1%	23%
Muscle Pain	1%	22%
Sinus Problems	1%	1%
Allergies	0%	0%
Bleeding Gums	0%	8%
Difficulty Concentrating	0%	27%
Dizziness	0%	0%
Hair Loss	0%	11%
Insomnia	0%	0%
Nausea	0%	0%
Weight Loss	0%	7%
People With No Chief Complaint	29%	
People With No Chief Or Any Complaint	11%	

Diagnostic Categories

The distribution of CCEP diagnoses according to International Classification of Diseases-Ninth Revision, Clinical Modification (ICD-9-CM)¹ coding categories is shown in Table 4. The ICD-9-CM coding system is the standard method used in medicine for classification of diseases, injuries, and symptoms.

In the CCEP, “Psychological Conditions” (19%), “Symptoms, Signs and Ill-Defined Conditions” (17%), and “Musculoskeletal System” (17%) represent the most frequent diagnostic categories, accounting for 53% of all primary diagnoses. Additionally, eleven percent (11%) of participants had diagnoses involving “V Codes”. “V Codes” are used to describe three groups of individuals in the CCEP: 1) those individuals without symptoms who request a medical evaluation, 2) those individuals with a normal medical evaluation, and 3) those individuals with a history of a preexisting condition but without a current illness. The average number of diagnoses per patient was three.

Of the 19% of CCEP participants with a primary diagnosis consisting of a “Psychological Condition,” four diagnoses represent 59% of this category: tension headache, major and minor depressive disorders, and prolonged posttraumatic stress disorder.

Of the 17% of the participants with a primary diagnosis within the ICD-9-CM category of “Symptoms, Signs, and Ill-Defined Conditions,” three diagnoses represent 63% of the total category and include: malaise and fatigue, sleep disturbance, and headache.

Table 4. Frequency Distribution of Primary and Any Diagnosis Among 10,020 Completed CCEP Evaluations (By ICD-9-CM Category)

Categories	Primary Diagnosis %	Any Diagnosis %
Psychological Conditions	19	37
Signs, Symptoms, and Ill Defined conditions ¹	17	41
Musculoskeletal	17	45
Healthy ²	11	19
Respiratory System	7	18
Nervous System	6	18
Digestive System	6	22
Skin & Subcutaneous	6	20
Infectious Disease	3	9
Endocrine	2	11
Circulatory System	2	8
Neoplasm	1	3
Genitourinary System	1	6
Injury and Poisoning	1	3
Congenital Anomalies and Conditions of the Perinatal Period	<1	<1
Total	100	N/A

¹Includes conditions categorized according to ICD-9 nomenclature consisting of cases for which no diagnosis is classifiable elsewhere; no more specific diagnosis can be made; signs or symptoms that prove to be transient; and, cases in which a more precise diagnosis was not available for any other reason.

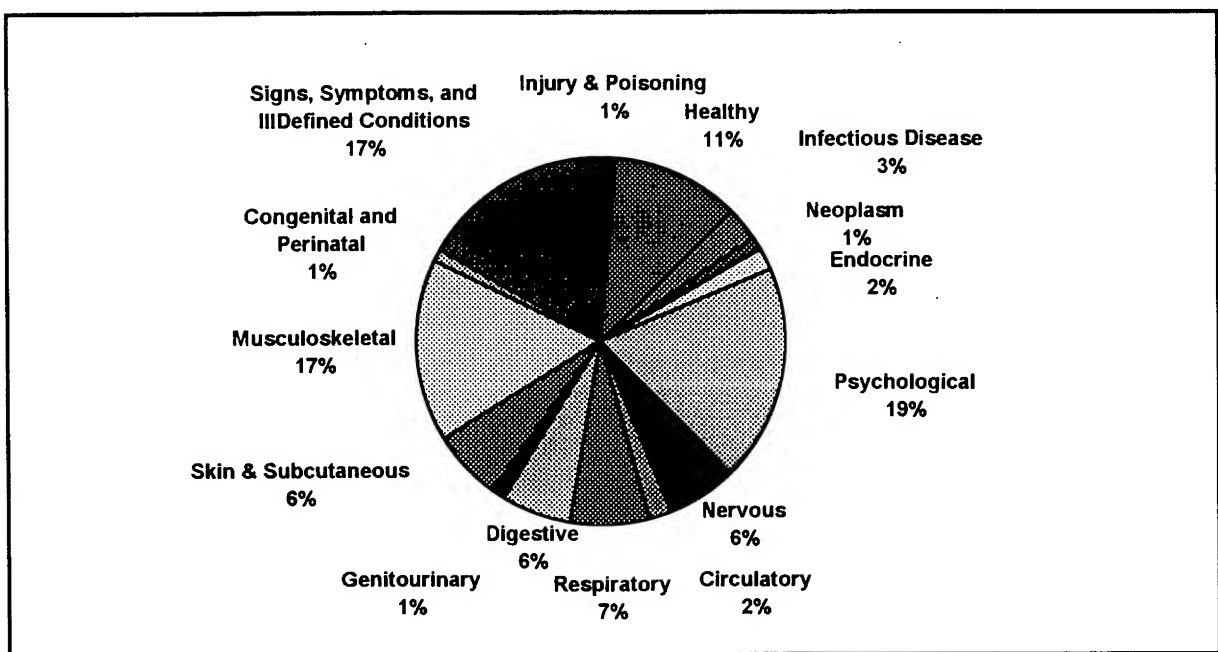
²Includes "V Codes" which refer to CCEP participants who: a) are seeking consultation without complaint or illness, b) are not currently sick, and/or c) have a circumstance or problem which influences a person's health status but is not in itself a current illness or injury

Of the 17% of CCEP patients with a primary diagnosis of "Musculoskeletal and Connective Tissue Conditions," three diagnoses represent 51% of the category: pain in joint (s), osteoarthritis, and backache/lumbago.

Neoplasms represent 1% of all primary diagnoses. Malignant disease was diagnosed in 56 (0.6 %) of all CCEP participants. The most frequently diagnosed malignant neoplasms were skin cancers (15 participants) and lymphoma (12 participants).

The frequency distribution of primary diagnoses is shown in Figure 2.

Figure 2. Distribution of Primary Diagnoses Among 10,020 CCEP Participants.



The CCEP database includes the records of 136 dependent spouses of Persian Gulf War veterans and 81 children. The distributions of diagnoses among spouses and children are shown in Table 5 and Table 6.

Table 5. Frequency Distribution of Primary and Any Diagnosis Among 136 Completed CCEP Evaluations of Spouses (By ICD-9-CM Category)

Diagnoses	Primary Diagnoses %	Any Diagnoses %
Psychological Conditions	24	41
Signs, Symptoms, and Ill defined conditions ¹	11	35
Skin & Subcut. Tissue	10	24
Healthy ²	10	20
Musculoskeletal/ Connective	9	32
Respiratory System	8	19
Nervous System	7	17
Digestive System	6	23
Endocrine	5	15
Genitourinary System	4	16
Infectious Diseases	2	7
Circulatory System	2	10
Neoplasm	1	4
Congenital Anomalies and Perinatal Conditions	1	3
Injury and Poisoning	0	0
Total	100	N/A

¹Includes conditions categorized according to ICD-9-CM nomenclature consisting of cases for which no diagnosis is classifiable elsewhere; no more specific diagnosis can be made; signs or symptoms that prove to be transient; and, cases in which a more precise diagnosis was not available for any other reason.

²Includes "V Codes" which refer to CCEP participants who: a) are seeking consultation without complaint or illness, b) are not currently sick, and/or c) have a circumstance or problem which influences a person's health status but is not in itself a current illness or injury.

Table 6. Frequency Distribution Of Primary Diagnoses Among 81 Children of Persian Gulf War Veterans in the CCEP

Diagnosis	Number
Healthy (Normal Exam)	17
Congenital Abnormalities*	15
Dermatitis, Eczema, Folliculitis, Acne	6
Asthma, Reactive Airway Disease	5
Other	5
Psychosis, Depression, Obsessive/Compulsive Disorder	4
Developmental Delay	4
Otitis Media	3
Upper Respiratory Infections	3
Rash	3
Nephritis, Vesicoureteral Reflux, Hydrocele	3
Tinea Capitis	2
Dermoid Cysts, Hemangiomas	2
Attention Deficit/Hyperactivity	1
Choroid Plexus Carcinoma	1
Anemia	1
Chronic Pneumonia	1
Chronic Diarrhea	1
Milk Allergy	1
Seizures	1
Insomnia	1
Static Encephalopathy of Childhood	1
Total	81

*Specific diagnoses include: Hydrocephalus (1), Glaucoma(1), Microsomia(1), Major Cardiac Anomalies(2), Cleft Palate(3), Trisomy 21(1), Fragile X Syndrome(1), Marcus-Gunn Syndrome(1), Pectus Excavatum(2), Left Hand Aphalangia(1), Omphalocele(1) These congenital abnormalities are based only on children whose parents chose to enroll them in the CCEP. Because of the self-selected nature of the CCEP and the absence of information concerning all births of Persian Gulf veterans, this data can not be used to determine a rate of birth defects that can be compared to a non-Persian Gulf population.

Self-Reported Work Days Lost Due to Illness

The CCEP questionnaire asks how many days of work the participant has lost because of illness within the last 90 days. Over 80% of participants reported not missing any work days in the 90 days prior to the evaluation. The percentage of participants reporting "0 days lost" did not differ greatly between ICD-9-CM categories (range: 75-90%). Among diagnostic categories, the

average number of work days lost ranged from 1-8, with "Neoplasms" representing the disease category with the greatest number of missed work days.

Satisfaction with CCEP

Approximately 64% of CCEP participants (6429/10020) responded to the question at the conclusion of their medical evaluation: "Were you satisfied with the care you received in the program?" Ninety one percent (91%) or (5853/6429) replied affirmatively. The satisfaction rate among respondents who completed Phase II evaluations was 97% (695/720) compared to 87% (5581/6380) for those who completed their evaluations at Phase I.

DISCUSSION

Epidemiological Considerations

The CCEP represents a large case series of over 10,000 comprehensive, systematic health evaluations. However, several methodological limitations associated with the CCEP need to be understood to interpret findings appropriately in this population. Since the CCEP represents individuals who have self-selected to enter the program and excludes individuals ineligible for care through the military medical system, it may not be totally representative of the overall population of veterans with health concerns of PGW veterans as a group.

The CCEP has conducted an aggressive campaign to provide medical examinations to Persian Gulf War veterans who believe they are experiencing medical problems related to their participation in the Gulf War. This pro-active "case finding" effort has resulted in the systematic evaluation of 10,020 patients, to date, including approximately 1700 intensive evaluations conducted at one of 15 tertiary care medical centers within the Military Health Services System. A case series, such as the CCEP, is not definitive in determining risk factors, causality or specifically defining associations, particularly when self-reported exposures cannot be validated. However, the CCEP does have utility in detecting a potential new clinical syndrome and in describing the nature of symptoms and illnesses in a very large group of veterans.

Comparison Group Selection

From an epidemiological perspective, either non-deployed Gulf War-era veterans or Gulf War-era veterans who experienced some other deployment represent appropriate groups for

comparative purposes. Studies of outpatient diagnoses for a population of non-deployed, Persian Gulf War-era veterans, while in progress, are incomplete at this time. However, for the purposes of the CCEP, until more definitive comparisons are made, use of both population-based surveys and examinations (e.g., National Ambulatory Medical Care Survey, National Institute of Mental Health Epidemiologic Catchment Area Studies, etc.), and other studies of symptoms and diagnoses in ambulatory patients, provide useful comparative information. Formal research efforts (which include appropriate control or comparison groups in their study design) by the Departments of Defense, Veterans Affairs and Health and Human Services (HHS) will, together with the CCEP, further characterize the health status of PGW veterans.

Demographics

Demographic variables of CCEP participants were compared with all who deployed to Operation Desert Shield/Desert Storm. A statistically significant difference was noted for each of the demographic variables with the exception of rank, Hispanic ethnicity, and Air Force affiliation. Given the self-selected nature of participants in the CCEP and eligibility criteria for access to DoD health care facilities, it is difficult to draw any meaningful conclusions from these differences, other than to say that CCEP participants are a non-random sample of the Persian Gulf War veteran population. The CCEP does, however, represent a somewhat balanced cross-section of all who deployed to the Gulf and there appear to be no unique characteristics among CCEP participants. Well-designed epidemiologic studies that compare the CCEP sub-population with an appropriately matched control population will provide the best information on which to base conclusions regarding demographics.

Unit Identification Codes - Specific Participation Rates

UIC specific CCEP participation rates indicated a low rate of CCEP participation in the great majority of UICs (mean 1.7 per 100 service members). This low rate of participation was present across a large range of UICs involving all services. The low "UIC-specific CCEP participation rates" across the wide range of UICs suggest that geographic clustering of illness did not occur. Although there appears to be no unique clustering of CCEP participants by UICs, the wartime and post-war experience of personnel within UICs with relatively higher rates of CCEP participation warrant further investigation.

would be represented in the CCEP. Injury and poisoning account for 10.7% of diagnoses in the NAMC but only 0.7% in the CCEP. Such patients are acutely ill or injured, come in promptly for care, and are treated within a matter of hours to a few days. Thus, they would be common in an office practice seeing acute and chronic patients but would be rare in a sample of patients with persistent symptoms, such as the CCEP. "V Codes" (Healthy) appear to be more common in the NAMCS because the leading reason for outpatient visits in the United States is general medical examinations, such as routine physicals for school, employment, or insurance purposes or annual "checkups" for health maintenance reasons. Asymptomatic patients coming in for routine physicals or simple checkups would be less prevalent in the CCEP. The higher percentage of genitourinary diagnoses in NAMCS may reflect the larger proportion of women in that survey compared to the CCEP and an increased prevalence of gender related diagnoses, such as bladder infections.

On the other hand, three diagnoses - "Psychological Conditions," "Symptoms, Signs and Ill-Defined Conditions", and "Musculoskeletal System" are more common in the CCEP than in NAMCS (53% vs. 17%). Possible explanations for the apparently higher prevalence of these diagnostic categories in the CCEP warrant discussion, which follows.

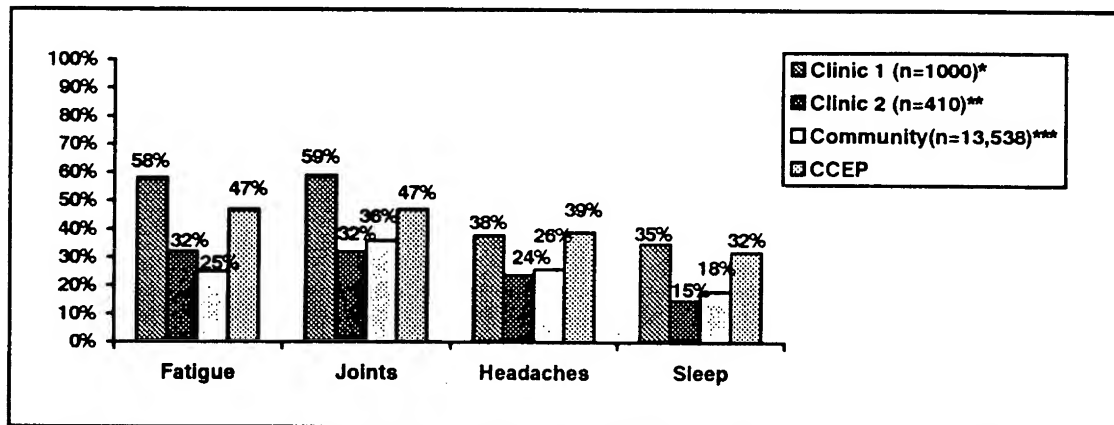
Use of Unit Identification Codes to Validate Self-Reported Exposures

Several of the potential exposures which occurred in the Persian Gulf (as self-reported by CCEP participants) were confined to units in specialized occupations or certain geographic locations. For example, malaria prophylaxis was provided only to selected units based upon geographic location. Similarly, anthrax and botulinum immunizations were restricted to certain units which were deployed forward in ODS/S. Analysis of the CCEP population by UIC-specific locations and military occupational specialty groups may enable validation of these and other exposures. The U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM) is currently integrating exposure data sets, troop movement data, and satellite imagery of the oil well fire period into a Geographic Information System (GIS) model thereby enabling spatial analyses. Additionally, analysis of classified and declassified operational, intelligence, medical sources of information, research databases, as well as anecdotal accounts of veterans will be correlated with findings of the CCEP and GIS to determine exposure relationships throughout the Persian Gulf theater of operations.

Symptoms

As shown in Figure 3, four of the most common symptoms reported by participants in the CCEP are also prevalent in the U.S. population as a whole and among patients in general medical practice. Three published surveys of outpatient practices are informative.^{20,21,22} Because the characteristics of the study groups and duration vary, exact comparisons of symptoms and illnesses can not be made among the three studies.

Figure 3. Common Symptom Prevalence as Reported in 3 Studies of Outpatient Practice in the United States, as Compared with CCEP



*Clinical Survey 1 = 1000 patients presenting for care at four primary care clinics in the U.S.

**Clinical Survey 2 = 410 patients attending a military general medicine clinic

***Community Survey 3 = Random survey of 13,538 persons in four communities in the U.S.

There appears, however, to be strong consistency of reported symptoms between large population studies of outpatient medical clinics and symptoms reported by CCEP participants. Referring to Figure 3, fatigue was reported by 22-58% (CCEP 47%) of respondents; joint pains by 26-59% (CCEP 47%); headaches by 21-37% (CCEP 39%), and sleep complaints by 15-35% (CCEP 32%). Not shown in Figure 3, but also very common in these surveys, were dyspnea for 14-32% (CCEP 16%) and abdominal pains for 11-24% (CCEP 16%).

The similarity of these particular CCEP symptoms in the U.S. general clinic population is further confirmed by examining data from the National Ambulatory Medical Care Survey (NAMCS). This national sample of medical clinics in the United States reported, that in 1989, the estimated number of outpatient visits in the United States was: 7 million visits for fatigue; 9.6 million visits for headaches; 17 million visits for joint pains; 14 million visits for skin rash; and 7 million visits for depression.

Patients commonly report experiencing multiple symptoms. Studies have shown that when patients complete symptom checklists one third of patients complain of 0-1 symptoms, one-third complain of 2-3 symptoms, and one-third complain of 4 or more symptoms.^{21,23} Research conducted by Kroenke et al indicates that typical outpatients will endorse a median of 4 symptoms as bothersome.^{22,24} CCEP patients reported an average of 5 symptoms per patient.

“Symptom syndromes”, i.e., illnesses manifested solely by combinations of symptoms with no consistent objective findings on physical examination or positive laboratory abnormalities and for which an adequate etiologic explanation is yet to be determined, are common in clinical practice and the general population. Symptom syndromes include entities such as irritable bowel syndrome, fibromyalgia, Chronic Fatigue Syndrome (CFS) and depression. Moreover, the overlap of specific symptoms can be considerable.^{25,26,27,28,29} For example, Table 7 compares the frequency of various symptoms seen in CCEP patients and three other common symptom syndromes.

Table 7. Prevalence of Various Symptoms in 3 Common Symptom Syndromes Compared with CCEP Patients

Symptom %	CCEP Patients (%)	CFS(%)	Fibromyalgia(%)	Major Depression(%)
Fatigue	47	100	85+	80+
Myalgia	47	40-50	100	40+
Headache	39	35-85	44-88	70+
Memory	33	50-85	-	80+
Sleep	32	15-90	56-80	80+
Depressed Mood	23	46-85	20-71	90+

Physical symptoms in both clinic patients and the general population frequently lack a clear-cut or definitive physical explanation or “cause.” Four community-based studies have shown that 20 to 75% of symptoms lack an association with a definitive diagnosis after a medical evaluation.^{20,22-24} The best estimate is that about one-third of symptoms cannot be linked to a defined diagnosis.

A recent study by the Centers for Disease Control and Prevention (CDC) compared the prevalence of symptoms in Persian Gulf veterans to non-deployed, Persian Gulf-era veterans.³⁰

Preliminary findings indicated that chronic symptoms, similar to those seen in CCEP participants, were reported more commonly by Persian Gulf veterans than non-deployed, Persian Gulf-era veterans. Comprehensive medical evaluations by CDC physicians and a review of medical records for fifty-nine Persian Gulf War veterans in the initial case series did not identify any consistent physical or laboratory abnormalities. A case-control study is currently being completed to compare symptoms and illnesses in deployed and non-deployed Persian Gulf War service members.

Existence of a Unique Illness

DoD physicians have diagnosed a wide range of medical conditions commonly seen in general medical practice, but have found no clinical evidence for a unique illness among CCEP participants. The large number of patients participating in the CCEP, the thoroughness of the evaluations, and the clinical impressions of CCEP physicians are the primary basis for forming conclusions regarding the existence of a new or unique condition or syndrome. Although CCEP physicians have not found clinical evidence for a unique illness or syndrome in examining individual patients, analysis of demographic, exposure, symptom and diagnostic results is useful in characterizing the nature of illnesses being experienced by Persian Gulf veterans participating in the CCEP.

CCEP Diagnoses Relative to Other Ambulatory Care Studies

The National Ambulatory Medical Care Survey (NAMCS) is considered the most representative study of outpatient medical practice in the U.S.³¹ It must be noted, however, that the NAMCS includes not only individuals with persistent symptoms but also patients with acute illnesses or injuries, healthy persons needing school physicals, employment or insurance examinations and other types of "walk-in" clinic visits. In contrast, the CCEP is more likely to include individuals with persistent symptoms and, as such, does not include patients whose symptoms typically are short-lived. Additionally, differences in the proportion of male and female participants in the two populations would contribute to differences in the size and composition of diagnostic categories. Therefore, because the populations differ, even general comparisons should be made with caution.

Generally speaking, the frequency distribution for a number of the ICD-9-CM codes appear similar in the NAMCS and CCEP patient populations (see Table 8), except for "Psychological Conditions," "Respiratory System," "Genitourinary System," "Musculoskeletal System," "Symptoms, Signs, and Ill-Defined Conditions," "Injury and Poisoning," and "V Codes" (Healthy).

Table 8. Frequency Distribution of Principal Diagnoses in U.S. Ambulatory Care Survey* (NAMCS) and in the CCEP

Frequency Distribution Of Principal Diagnoses In United States Ambulatory Care (NAMCS) And In The CCEP			
Primary Diagnoses	ICD-9-CM	NAMCS ¹	CCEP
		--Percent Distribution--	
Infectious Diseases	001-139	3.5	2.9
Neoplasms	140-239	2.4	1.1
Endocrine	240-279	3.0	1.8
Psychological conditions	290-319	6.0	18.6
Nervous System	320-389	6.5	5.4
Circulatory System	390-459	3.1	2.2
Respiratory System	460-519	11.7	6.7
Digestive System	520-579	3.8	6.4
Genitourinary System	580-629	8.1	1.5
Skin & Subcut. Tissue	680-709	5.8	6.3
Musculoskeletal System & Connective Tissue	710-739	6.8	17.0
Symptoms, Signs & Ill-Defined Conditions	780-799	4.1	17.5
Injury And Poisoning	800-999	10.7	0.7
"V Codes" (Healthy)		19.9	10.9
All other Diagnoses ¹		2.3	1.0
Unknown or blank ²		2.3	0.0

*NAMCS data for ages 25-44

¹Includes diseases of the blood and blood-forming organs (280-288)/complications of pregnancy, childbirth, and the puerperium (630-676); congenital anomalies (740-759); and certain conditions originating in the perinatal period (760-779).

²Includes blank diagnoses, uncodable diagnoses, and illegible diagnoses.

For purposes of general comparison, respiratory system diagnoses appear to occur more commonly in the NAMCS (11.7% vs. 6.7%), probably because upper respiratory illnesses (URI's), such as the common cold, are one of the leading reasons for outpatient visits in the United States. Because URI's typically resolve in a week or less, very few patients with URI's

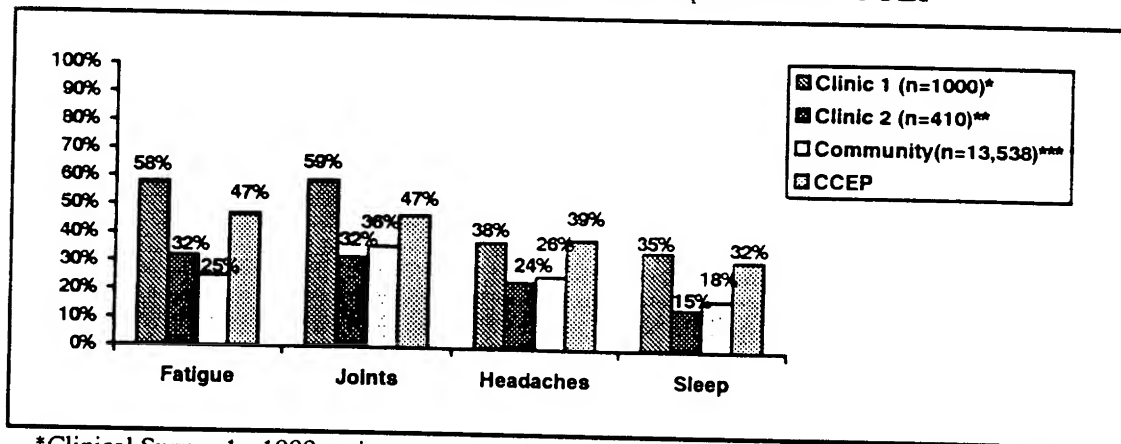
Use of Unit Identification Codes to Validate Self-Reported Exposures

Several of the potential exposures which occurred in the Persian Gulf (as self-reported by CCEP participants) were confined to units in specialized occupations or certain geographic locations. For example, malaria prophylaxis was provided only to selected units based upon geographic location. Similarly, anthrax and botulinum immunizations were restricted to certain units which were deployed forward in ODS/S. Analysis of the CCEP population by UIC-specific locations and military occupational specialty groups may enable validation of these and other exposures. The U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM) is currently integrating exposure data sets, troop movement data, and satellite imagery of the oil well fire period into a Geographic Information System (GIS) model thereby enabling spatial analyses. Additionally, analysis of classified and declassified operational, intelligence, medical sources of information, research databases, as well as anecdotal accounts of veterans will be correlated with findings of the CCEP and GIS to determine exposure relationships throughout the Persian Gulf theater of operations.

Symptoms

As shown in Figure 3, four of the most common symptoms reported by participants in the CCEP are also prevalent in the U.S. population as a whole and among patients in general medical practice. Three published surveys of outpatient practices are informative.^{20,21,22} Because the characteristics of the study groups and duration vary, exact comparisons of symptoms and illnesses can not be made among the three studies.

Figure 3. Common Symptom Prevalence as Reported in 3 Studies of Outpatient Practice in the United States, as Compared with CCEP



*Clinical Survey 1 = 1000 patients presenting for care at four primary care clinics in the U.S.

**Clinical Survey 2 = 410 patients attending a military general medicine clinic

***Community Survey 3 = Random survey of 13,538 persons in four communities in the U.S.

There appears, however, to be strong consistency of reported symptoms between large population studies of outpatient medical clinics and symptoms reported by CCEP participants. Referring to Figure 3, fatigue was reported by 22-58% (CCEP 47%) of respondents; joint pains by 26-59% (CCEP 47%); headaches by 21-37% (CCEP 39%), and sleep complaints by 15-35% (CCEP 32%). Not shown in Figure 3, but also very common in these surveys, were dyspnea for 14-32% (CCEP 16%) and abdominal pains for 11-24% (CCEP 16%).

The similarity of these particular CCEP symptoms in the U.S. general clinic population is further confirmed by examining data from the National Ambulatory Medical Care Survey (NAMCS). This national sample of medical clinics in the United States reported, that in 1989, the estimated number of outpatient visits in the United States was: 7 million visits for fatigue; 9.6 million visits for headaches; 17 million visits for joint pains; 14 million visits for skin rash; and 7 million visits for depression.

Generally speaking, the frequency distribution for a number of the ICD-9-CM codes appear similar in the NAMCS and CCEP patient populations (see Table 8), except for "Psychological Conditions," "Respiratory System," "Genitourinary System," "Musculoskeletal System," "Symptoms, Signs, and Ill-Defined Conditions," "Injury and Poisoning," and "V Codes" (Healthy).

Table 8. Frequency Distribution of Principal Diagnoses in U.S. Ambulatory Care Survey* (NAMCS) and in the CCEP

Frequency Distribution Of Principal Diagnoses In United States Ambulatory Care (NAMCS) And In The CCEP			
Primary Diagnoses	ICD-9-CM	NAMCS ¹	CCEP
		--Percent Distribution--	
Infectious Diseases	001-139	3.5	2.9
Neoplasms	140-239	2.4	1.1
Endocrine	240-279	3.0	1.8
Psychological conditions	290-319	6.0	18.6
Nervous System	320-389	6.5	5.4
Circulatory System	390-459	3.1	2.2
Respiratory System	460-519	11.7	6.7
Digestive System	520-579	3.8	6.4
Genitourinary System	580-629	8.1	1.5
Skin & Subcut. Tissue	680-709	5.8	6.3
Musculoskeletal System & Connective Tissue	710-739	6.8	17.0
Symptoms, Signs & Ill-Defined Conditions	780-799	4.1	17.5
Injury And Poisoning	800-999	10.7	0.7
"V Codes" (Healthy)		19.9	10.9
All other Diagnoses ¹		2.3	1.0
Unknown or blank ²		2.3	0.0

*NAMCS data for ages 25-44

¹Includes diseases of the blood and blood-forming organs (280-288)/complications of pregnancy, childbirth, and the puerperium (630-676); congenital anomalies (740-759); and certain conditions originating in the perinatal period (760-779).

²Includes blank diagnoses, uncodable diagnoses, and illegible diagnoses.

For purposes of general comparison, respiratory system diagnoses appear to occur more commonly in the NAMCS (11.7% vs. 6.7%), probably because upper respiratory illnesses (URI's), such as the common cold, are one of the leading reasons for outpatient visits in the United States. Because URI's typically resolve in a week or less, very few patients with URI's

would be represented in the CCEP. Injury and poisoning account for 10.7% of diagnoses in the NAMC but only 0.7% in the CCEP. Such patients are acutely ill or injured, come in promptly for care, and are treated within a matter of hours to a few days. Thus, they would be common in an office practice seeing acute and chronic patients but would be rare in a sample of patients with persistent symptoms, such as the CCEP. "V Codes" (Healthy) appear to be more common in the NAMCS because the leading reason for outpatient visits in the United States is general medical examinations, such as routine physicals for school, employment, or insurance purposes or annual "checkups" for health maintenance reasons. Asymptomatic patients coming in for routine physicals or simple checkups would be less prevalent in the CCEP. The higher percentage of genitourinary diagnoses in NAMCS may reflect the larger proportion of women in that survey compared to the CCEP and an increased prevalence of gender related diagnoses, such as bladder infections.

On the other hand, three diagnoses - "Psychological Conditions," "Symptoms, Signs and Ill-Defined Conditions", and "Musculoskeletal System" are more common in the CCEP than in NAMCS (53% vs. 17%). Possible explanations for the apparently higher prevalence of these diagnostic categories in the CCEP warrant discussion, which follows.

Psychological Conditions

Psychiatric disorders such as depression, anxiety, and somatoform disorders are common in primary care, existing in 25-35% of all patients presenting for care in the outpatient setting.^{32,33} Overall prevalence of psychological conditions among CCEP patients (19% primary, 37% any diagnosis) may be somewhat higher than that found for other groups of health care seeking individuals (Table 9) in which structured psychiatric interviews were used.

Table 9. Prevalence Of Psychological Conditions In CCEP Participants Compared To Other Community And Primary Care Cohorts

Sample Source	Prevalence of Psychological Conditions (All Conditions)
Midtown Manhattan Study (Community)	23%*
NIMH Epidemiologic Catchment Area Studies (Community)	18-27%
Primary Care	25%-35%
CCEP	19-37%

*percentage of respondents with "serious impairment".

The most common psychological conditions among CCEP patients are: somatoform problems, especially tension headache; nonspecific, mild, or stress-related anxiety and/or depression; posttraumatic stress disorder, and alcohol-related disorders. None of these disorders was noticeably more prevalent than available figures from previous community and primary care based studies (see Table 10).^{34,35}

Table 10. Most Common Psychological Conditions Among CCEP Participants, General Population And Primary Care Patients

Psychological Condition	CCEP		General Pop'n	Primary Care
	Primary Dx	All Dx		
Somatoform Problems	5%	15%	---	---
Somatization Disorder	0.8%	2%	0.1-1%	1-5%
Tension Headache	4%	12%	20%	---
Mood Depression	6%	12%	4-6%	15-25%
Major Depressive Disorder	2%	3%	2-5%	5-14%
Mild Depressive Syndrome	4%	8%	7%	---
Anxiety Disorders	4%	8%	7%	5-15%
Posttraumatic Stress Disorder	3%	5%	1-14%	---
Mild Anxiety Syndromes	0.6%	2%	---	---
Adjustment Disorders	2%	4%	---	---
Substance Related Disorders	0.5%	2%	---	---
Alcohol Related Disorders	0.4%	2%	4-6%	6%

Psychological conditions may be more common in the CCEP because patients with persistent or unexplained symptoms have high rates (50% or more) of underlying mood or anxiety disorders. This need not always mean that the symptoms are caused by the mood or anxiety disorder since it is possible that depression or anxiety can be a consequence of persistent, disabling physical symptoms. Nonetheless, the mood or anxiety disorders that coexist in half or more of such patients can further aggravate such symptoms through worsening sleep, increased fatigue, lowered pain tolerance, and mental suffering.

Ill-Defined Signs and Symptoms

Approximately 17% of CCEP participants have primary diagnoses categorized by the ICD-9-CM as “Signs, Symptoms and Ill-Defined Conditions.” Although an illness or symptom may fall in the 780-799 ICD-9-CM code range, that code may represent a well-defined condition not classified elsewhere (e.g., obstructive sleep apnea) or a nonspecific laboratory abnormality (e.g., elevated sediment rate). Also, patients with persistent symptoms in whom physical examination and diagnostic testing is normal often end up with a “symptomatic” diagnosis (e.g., lower back pain, headache, sleep disturbance, fatigue) rather than a more precise, anatomic or pathophysiologic diagnosis.

Depression and anxiety show a particularly strong association with unexplained or ill-defined physical symptoms. Studies have demonstrated that ill-defined (compared with better-defined) symptoms or syndromes tend to occur much more frequently in individuals with common, treatable anxiety and depressive disorders.^{21,22} Treatment of depression and anxiety is known to decrease the severity of physical symptoms.

The higher proportion of “ill-defined diagnoses” (as compared with the NAMCS) is consistent with the earlier observations that the CCEP preferentially selects for patients with persistent symptoms and underrepresents those with acute, self-limited illnesses.

Musculoskeletal Conditions

Seventeen percent (17%) of CCEP participants had a primary diagnosis of musculoskeletal/connective tissue disorders. Forty-two percent (42%) of the diagnoses in this category consist of pain in joint, osteoarthritis, and unspecified arthropathy. Osteoarthritis is commonly the chronic result of occupational and recreational overuse injuries. Such injuries frequently occur as a consequence of the physical activity associated with military operations and training. Review of military disability evaluation system information confirms that musculoskeletal conditions are a leading category of disability in the Armed Forces. Musculoskeletal impairments are among the most common and disabling of medical disorders.³⁶ Therefore, the increased prevalence of musculoskeletal conditions in the CCEP relative to NAMCS may be related to the physical demands military service.

Additional Diagnostic Considerations

Infectious diseases and conditions associated with symptoms of fatigue, sleep disturbances and memory loss are of special concern and warrant further discussion.

Infectious Diseases

The threat to deployed military personnel posed by infectious diseases was recognized and preparations were made from the earliest stages of Operation Desert Shield.³⁷ Specific infectious diseases observed in U.S. troops during Operations Desert Shield/Storm conformed with expected disease threats. Data suggest that overall exposure to recognized pathogens was quite low. Furthermore, it suggests that no route of infection, other than ingestion of locally-procured food, was common. The reported incidence of infectious diseases observed during the Operations is relevant to evaluation of current health complaints of Gulf War veterans.

Leishmaniasis has been one of the infectious diseases of particular concern in evaluating Persian Gulf veterans. Since the Gulf War a total of 31 cases of leishmaniasis have been identified among Persian Gulf veterans (12 cases of viscerotropic disease and 19 cases of cutaneous disease).³⁸ Virtually all of these cases were identified prior to initiation of the CCEP, and none was identified by the CCEP. All but one of the cases were characterized by the presence of objective findings on physical examination or screening laboratory assays. The low incidence of leishmaniasis during and immediately after Operations Desert Shield/Storm, the absence of other sandfly-borne diseases in our troops, and the low prevalence of objective findings pointing to leishmanial disease among 10,000 CCEP patients, all indicate that viscerotropic leishmaniasis plays no significant role in the current complaints of Gulf War veterans.

The CCEP itself has identified a wide variety of infectious diagnoses. Of these, by far the largest group has been fungal infections of the skin due to fungi common in the United States. Virtually all of the remaining infections have represented common illnesses, such as sinusitis, diarrheas, and a few cases of viral hepatitis, not specific to the Persian Gulf region. The overwhelming majority of these diagnoses represent incidental diagnoses which would not explain persistent systemic complaints.

Fatigue

Chronic Fatigue Syndrome (CFS) has been suggested as a unifying diagnosis for unexplained illnesses among Persian Gulf veterans. Complaints of chronic fatigue lasting greater than six months are not uncommon in the general population seeking medical care^{39,40} However, patients meeting the Chronic Fatigue Syndrome case definition are relatively rare. Records of 4.6% (464/10,020) of the CCEP patients carried a primary diagnosis of "fatigue" (ICD-9-CM 780.7 - 780.79). These records were reviewed to determine if they met the 1994 CDC case definition of CFS. Forty-two of the 464 participants with a primary diagnosis of fatigue (9 %) met the case definition. This represents a prevalence in the CCEP study population of 0.42% (42/10,020). This rate is similar to the prevalence rate of 0.3% reported in a general medical population.

An additional syndrome Fibromyalgia Syndrome (FMS) is often mentioned together with CFS because fatigue is prominent among the somatic symptoms seen with this entity. The definition for FMS has been published by the American College of Rheumatology.⁴¹ CCEP records were examined for FMS in both primary and secondary diagnoses. Fibromyalgia was found as the primary diagnosis in 78 of 10,020 individuals (0.78%) and in 175 individuals (1.75%) in primary or secondary diagnoses. These prevalence rates are consistent with those seen in the U.S. population.

Sleep

Sleep disturbances represent medical conditions which can be systematically evaluated and treated. Sleep disturbance was the fifth most common complaint among CCEP participants, with 32% reporting this symptom. Epidemiological surveys of the general population yield similar results of subjects reporting sleep problems ranging from 30-40%. A recent Gallop survey based on 1,950 phone interviews found that 36% of Americans suffer from some type of sleep problem.⁴² Substantial numbers of sleep disorders (ICD-9-CM 307.4, 780.5) were found in the CCEP participants, with 357 (4%) having a sleep disorder as the primary diagnosis. Sleep disorders most frequently diagnosed in the CCEP participants were sleep apnea and disorders involving initiating and maintaining sleep (insomnias). The prevalence of sleep disorders in CCEP participants did not exceed that expected for the general population.^{43,44}

The common sequelae resulting from these sleep disorders is chronic sleep deprivation. It is well documented that chronic sleep deprivation can lead to various physical and psychological complaints, many of which are the same as described by the CCEP participants (See Table 3).⁴⁵ Evidence from epidemiological studies suggests a strong association between sleep and other somatic complaints, though there is no clear cause-and-effect relationship.⁴⁶

Memory Problems

Memory problems are a frequent complaint associated with the medical conditions diagnosed among the Persian Gulf veterans. They are the fourth most common symptom among CCEP participants. Memory is not an isolated function, but rather a complex of neurobiological and neuropsychological processes. It represents one of the neurobehavioral functions most sensitive to central nervous system disruption.⁴⁷ In-depth neuropsychological evaluations in the CCEP population have identified no evidence of an increased prevalence of neurologic etiologies for memory loss. Organic mental disorders (ICD-9-CM code 310.1, 310.1, 310.8, 310.9) confirmed by neuropsychological testing and evaluation were found in only 0.6% of CCEP participants, which is less than expected within the general population.

Patients with depression, sleep disorders, chronic fatigue, and chronic pain often complain of memory problems.^{48,49,50} These medical conditions represent potentially treatable causes of memory complaints.

Diagnoses in Spouses and Children

Some Gulf War veterans have expressed concern that the health of their spouses and children may have been affected by their military service in the Gulf War. The spectrum of diagnoses in spouses and children (Tables 5 and 6) spans a wide range of organ systems. Although relatively few spouses have enrolled in the CCEP, the distribution of their diagnoses is consistent with the types of conditions commonly seen in clinical practice and seen in CCEP participants overall. Likewise, the diagnoses of children enrolled in the CCEP appears to be similar to that seen in pediatric practice. As the number of these self-referred spouses and children in the CCEP cohort is small, comparisons with other study groups would not yield worthwhile results.

Reproductive Health Concerns

Some Persian Gulf War veterans have reported adverse birth outcomes and reproductive problems. The CCEP includes 15 children with congenital abnormalities whose parents chose to enroll them in the program. These birth defects span a wide range of conditions which are not concentrated in any single organ system or congenital syndrome. Because of the self-selected nature of the CCEP and the absence of information about a representative sample of births of all Persian Gulf veterans, data are insufficient to determine a rate of birth defects that can be compared to a non-Persian Gulf population.

Investigations by state and national public health agencies and DoD have identified no elevated rates or unusual patterns of birth defects in babies born to Gulf War veterans or their spouses.^{51,52,53} In response to veterans' concerns, specific questions regarding reproductive history were added to the revised CCEP questionnaire in February, 1995. Less than 8% of the CCEP records in this report contained self-reported reproductive history; therefore, analysis has been deferred to future reports. However, to date, the birth defects which have been documented in pediatric CCEP participants are few in number and dissimilar in type. Population-based reproductive health outcome studies currently in progress will provide a more definitive assessment of possible reproductive health consequences related to service in the Persian Gulf War.

Disability

As an approximation of severity of morbidity and/or acute disability, "lost work days due to illness in the past 90 days" were obtained. Most CCEP participants (81%) did not report missed work due to illness or injury during the 90 days prior to their initial evaluation. The distribution of "lost work days" did not vary substantially among different disease categories. Seven percent of CCEP participants self-reported missing more than one week of work due to illness during the previous 90 days. Sixty-one participants reported not working during the entire 90 day period; 19 individuals had psychological conditions and 12 individuals had diagnoses in the "Symptoms, Signs and Ill-Defined Conditions" category. Although absenteeism is only one marker for the assessment of disability, the data suggest that few CCEP participants are experiencing disabling symptoms severe enough to interfere with work.

Patient Satisfaction

In an effort to assess satisfaction with the CCEP, participants were asked whether or not they were satisfied with the CCEP program. Of the 65% of patients who answered the question regarding satisfaction, 91% were satisfied with the care received in the program. Percentages did not differ among the subsets of patients with a 780-799 ICD-9-CM diagnosis (90%), and "V Codes", (healthy) diagnosis (92%), or a mental disorder diagnosis (90%). By comparison, in the largest national study of outpatient satisfaction to date (the Medical Outcomes Study involving 17,671 patients), the percentage of patients rating their care as very good to excellent was 87% overall, but in managed care settings (the system most similar to the military health care system), the percent satisfied was somewhat lower.² In general, the satisfaction ratings concerning the care received in the CCEP are similar to satisfaction surveys in the civilian sector.

Additional Research Efforts

The CCEP and the VA Persian Gulf Health Registry are providing information about the types of symptoms and illnesses experienced by Gulf War veterans. However these clinical programs are not able to fully determine the prevalence, incidence, or risk factors of disease related to ODS/S deployment. Therefore, an extensive research program has been initiated by DoD, DVA, and HHS which will complement registry findings.⁵⁵ Among the efforts in process, are three major epidemiological studies being conducted by the Naval Health Research Center, the CDC, and the DVA. The Naval Health Research Center, San Diego, CA (in collaboration with the DVA, HHS, and the University of California), is conducting a series of epidemiological studies of active duty military personnel. Studies include personal interviews and physiologic testing of 750 ODS/S veterans and 1500 non-deployed Gulf-era veterans; analysis of the hospitalization records of 1.2 million service members; and review of pregnancy outcomes among Gulf War veterans and their spouses. Initial findings from these studies are expected in late 1995.

The DVA Environmental Epidemiology Service, Washington, DC, (in collaboration with DoD and HHS) is planning a random survey of 15,000 veterans who served in the Persian Gulf and 15,000 "control" era veterans. This mail/telephone survey is designed to: a) describe symptomatology experienced after Gulf service; b) assess the current health status of veterans

and their family members, including reproductive health; and, c) evaluate the risk of potential environmental exposures.

The CDC is also planning to investigate the prevalence of reported symptomatology, illnesses, and exposures among Persian Gulf service members who list Iowa as their home of record.

Other ongoing research studies will further assess reproductive health, evaluate new diagnostic tests for infection, and study the health effects of exposure to depleted uranium and possible interactive effects of chemical exposures. This extensive research program will provide a comprehensive evaluation of the health consequences of Persian Gulf service and will contribute to the development of programs to protect the health of military personnel during future deployments.

The information maintained in the CCEP database constitutes a large case series, and was not designed to be a research study. Nevertheless, the CCEP database provides valuable descriptive information and, as such, is useful for generating hypotheses for future research. Once privacy act provisions have been met which ensure the protection of individual participants, the entire CCEP data set will be placed in a format that will allow access to a broad range of scientific investigators. The DoD anticipates working on this project with the National Technical Information Service through the Defense Technical Information Center.

Individual and Group Response to Environmental Hazards as a Factor Contributing to Health Consequences Among CCEP Participants

Fatigue, stress, fear, sleep disturbances, posttraumatic stress symptoms, anxiety and depression are common conditions which have been observed among military populations after participation in armed conflicts^{56,57,58,59,60} as well as persons who have experienced natural and manmade disasters.⁶¹ Such physical and psychological effects may persist long after a disaster has occurred. War is one of the most complex of the man made environmental disasters.⁶² Persian Gulf War veterans experienced the hazards of war which are always associated with combat. In addition, they experienced the unique environmental exposures and threats of exposure of the Persian Gulf, (e.g., the Kuwaiti oil well fires). Combat stressors (environmental exposures and

the threat of environmental hazards) are complex events with multiple physiological, psychological and social responses in individuals who experience them.⁶³

Service in the Persian Gulf involved numerous stressors, i.e., infectious diseases, chemicals, radiation, smoke from oil well fires, and possible reactions to prophylactic drugs and vaccines. For many, the threat of an environmental hazard was ever present.

It is clear that the Persian Gulf War experience itself, combined with an atmosphere of uncertainty concerning possible health consequences, has resulted in stress for many CCEP participants. The experience of environmental threat or the threat of a disaster can be very important in determining chronic stress and mental health effects. People may experience symptoms which are a direct result of exposure and/or threat of exposure. An individual will often link symptoms to an exposure threat.

The CCEP has identified/confirmed symptoms and diagnosable diseases, both physical and psychological, that would be expected in a general population. Psychiatric diagnoses account for 19% of all primary diagnoses in the CCEP. These diagnoses reflect both expected rates in the general population and the influence of chronic stress on this group of patients as a result of their concerns about exposures. Further research on the relative impact of the Gulf War experience in terms of development of medical conditions seen in the CCEP will require epidemiologic studies involving appropriate comparison groups.

CONCLUSIONS

The large size of the CCEP cohort and the thoroughness of CCEP examinations provide considerable clinical insight for understanding the nature of illnesses and health complaints being experienced by this group of veterans. However, self-selection of patients, differential eligibility, recall bias, inability to validate self-reported exposures, and lack of an appropriate control group limit the generalization of these findings to other Gulf War veterans.

The CCEP has conducted an aggressive campaign to provide medical examinations to Persian Gulf War veterans who believe they are experiencing medical problems related to their participation in the Gulf War. This pro-active "case finding" effort has resulted in the systematic evaluation of 10,020 patients, to date, including approximately 1700 intensive evaluations at one of 15 tertiary care medical centers within the Military Health Services System. The large number

of patients participating in the CCEP, the thoroughness of the evaluations, and the clinical impressions of CCEP physicians are the primary basis for conclusions regarding the lack of existence of a new or unique condition or syndrome.

Based on the CCEP experience to date, there exists no clinical evidence for a new or unique illness or syndrome among Persian Gulf veterans. DoD physicians have diagnosed a wide range of medical conditions commonly seen in general medical practice. The results of the CCEP are consistent with conclusions of a National Institutes of Health Technology Assessment Workshop that "no single disease or syndrome is apparent, but rather multiple illnesses with overlapping symptoms and causes." Although CCEP physicians have found no clinical evidence for a unique illness or syndrome, the analysis of demographic information, exposure data, symptoms, and diagnostic results, are useful in characterizing the types of illnesses being experienced by Persian Gulf veterans participating in the CCEP.

In general, there appear to be no unique distinguishing characteristics of CCEP participants. CCEP participants served in a large number of units during the Persian Gulf. Preliminary analysis indicates no apparent clustering of CCEP participants on the basis of unit of assignment during the Gulf War. The exposures which CCEP participants describe span a wide range of occupational and environmental chemical/physical agents, vaccines and medications. Confirmation of these exposures was not within the scope of the CCEP, since the primary objective of the exposure questionnaire was to assist the physician in the diagnosis of the patient's medical condition. However, in specific instances, exposures are known to have been limited to relatively small numbers of individuals (e.g., depleted uranium, malaria prophylaxis, and botulinum toxoid).

CCEP participants commonly report experiencing symptoms of fatigue, joint pain, headache, and sleep disturbances. Review of studies of patients with similar chronic health complaints seeking primary care in the U.S. indicate these symptoms are routinely reported and are not unique to CCEP participants. Although the types of symptoms being experienced by CCEP participants are not unique, studies using appropriate control populations will determine whether these symptoms are associated with greater illness in subsets of Persian Gulf veterans than might be expected.

The CCEP has identified a wide range of primary diagnoses commonly seen in clinical practice (e.g., tension headache, migraine headache, fatigue, osteoarthritis, back pain, depression and stress related conditions). Using standard ICD-9-CM coding criteria, 51% of the CCEP diagnoses can be classified as "Psychological Conditions," "Signs, Symptoms, Ill-Defined Conditions," and "Musculoskeletal & Connective Tissue." Review of NAMCS data suggests that these diagnostic categories may be over represented in the CCEP. Potential explanations for these differences include, but are not limited to: 1) aggressive "case finding" which has attracted Persian Gulf war veterans with chronic, non-specific symptoms; 2) selection of individuals with background physical conditions (musculoskeletal injuries) associated with the physical demands of military service; 3) use of a structured, in-depth protocol to diagnose physiologic and psychological conditions which might otherwise not be evident in the course of routine, primary care; and, 4) factors directly related to the Persian Gulf War experience, such as exposure to stressful circumstances.

Concern regarding the possible existence of "unexplained illnesses" was a major consideration in the design of the CCEP. Although CCEP physicians have not identified a unique illness or syndrome, 17% of CCEP primary diagnoses can be categorized as "Signs, Symptoms and Ill-Defined Conditions" according to ICD-9-CM coding criteria. It should be noted that these diagnoses refer to a variety of conditions (well-defined conditions not classified elsewhere in the ICD-9-CM system, generalized symptoms, nonspecific findings, and abnormal laboratory tests) commonly encountered in primary care medical practice. As previously discussed, physical symptoms in both clinic patients and the general population frequently lack a clear-cut or discrete physical explanation or "cause." Coding of a diagnosis within the category of "Signs, Symptoms and Ill-Defined Conditions" primarily reflects limitations in diagnostic and/or coding criteria rather than an impression as to whether or not the condition can be explained.

Severe disability measured in terms of lost work days is not a major characteristic of CCEP participants. Some CCEP patients with severe disability may benefit from participation in special programs which focus on rehabilitation, restoration of function and promotion of general well being. The DoD has established Specialized Care Centers, staffed by interdisciplinary teams, to provide such programs.

References

1. Persian Gulf Veterans Coordinating Board. Unexplained illnesses among Desert Storm Veterans. *Arch Intern Med* 1995;155:262-268..
2. U.S. Army Medical Research, Development, Acquisition and Logistics Command (Provisional). The General Well-Being Of Gulf War Era Service Personnel From The States Of Pennsylvania And Hawaii: A Survey. 1994. Office of the Assistant Secretary of Defense - Health Affairs, the Pentagon, Arlington, VA.
3. Ross MC, Wonders J. An exploration of the characteristics of post-traumatic stress disorder in reserve forces deployed during Desert Storm. *Arch Psychiatr Nurs* 1993;7:265-269.
4. Perconte ST, Dietrick AL, Wilson AT, Spiro KJ, Pontius EB. Psychological and war stress symptoms among deployed and non-deployed reservists following the Persian Gulf war. *Mil Med* 1993;158:516-521.
5. Sutker PB, Uddo M, Brailey K, Allain An. War-zone trauma and stress-related symptoms in Operation Desert Shield/Storm (ODS) returnees. *J Soc Issues* 1993;49:33-49.
6. Report of the Defense Science Board Task Force on Persian Gulf War Health Effects, June 1994. Office of the Under Secretary of Defense for Acquisition and Technology. Washington, DC 20301-3140.
7. National Institutes of Health Technology Assessment Workshop Panel. The Persian Gulf Experience and Health. *JAMA* 1994;272:391-395.
8. Dunn MA, Sidell FR. Progress in medical defense against nerve agents. *JAMA* 1989;262:649-652.
9. Sharabi Y, Danon YL, Berkenstadt H, Almog S, Mimouni-Bloch A, Zisman A, Dani S, Atsomon J. Survey of symptoms following intake of pyridostigmine during the Persian Gulf war. *Isr J Med Sci* 1991;27:656-658.
10. Cook JE, Wenger CB, Kolka MA. Chronic pyridostigmine bromide administration: Side effects among soldiers working in a Desert Environment. *Mil Med* 1992;157:250-254.
11. Keeler JR, Hurst CG, Dunn MA. Pyridostigmine used as a nerve agent pretreatment under wartime conditions. *JAMA* 1991;266: 693-695.
12. Brachman PS, Gold H, Plotkins SA, Fekety FR, Werrin M, Ingraham NR. Field evaluation of a human anthrax vaccine. *Am J Pub Health* 1962;52:632-645.
13. White CS, Adler WH, McGann VG. Repeated Immunization: Possible adverse effects: Reevaluation of human subjects at 25 years. *Ann Intern Med* 1974;81:594-600.
14. Hyams KC, Hanson K, Wigall FS, Escamilla J, Oldfield EC. The impact of infectious diseases on the health of U.S. troops deployed to the Persian Gulf during Operations Desert Shield and Desert Storm. *Clin Infect Diseases*. 1995;20:1497-1504.
15. Magill AJ, Grogil M, Gasser RA, Sun W, Oster CN. Visceral infection caused by Leishmani tropica in veterans of Operation Desert Storm. *N Engl J Med* 1993;328:1383-1387.
16. Executive Summary, Final Report: Kuwait oil fire health risk assessment, No. 39;26-L192-91, 5 May - 3 December 1991. Department of the Army, U.S. Army Environmental Hygiene Agency, Aberdeen Proving Ground, MD 21010-5422.
17. Report to Congress, United States Gulf Environmental Technical assistance, January 27-July 31, 1991, U.S. Environmental Protection Agency. Gulf Task Force, EPA, Washington, DC 20460.
18. Korenyi-Both AL, Molnar AC, Korenyi-Both AL, Fidelu-Gort RF. Al Eskan disease: Desert Storm pneumonitis. *Mil Med* 1992;157:452-462.
19. United States National Center for Health Statistics. International Classification of Diseases, 9th Revision, Clinical Modification. 1980;Vols 1-3.
20. Kroenke K, Price R. Symptoms in the community: prevalence, classification, and psychiatric comorbidity. *Arch Intern Med* 1993;153:2474-2480.
21. Kroenke K, Arrington ME, Mangeisdorff AD. The prevalence of symptoms in medical outpatients and the adequacy of therapy. *Arch Intern Med* 1990;160:1685-1689.
22. Kroenke K, Spitzer RL, Williams JBW, et al. Physical symptoms in primary care: predictors of psychiatric disorders and functional impairment. *Arch Fam Med* 1994; 3:774-779.
23. Reidenberg MM, Lowenthal DT: Adverse mondrug reactions. *N Engl J Med* 1968; 279:678-679
24. Marple R, Lucey C, Kroenke K, et al. A prospective study of the concerns and expectations in patients presenting with common symptoms; and The 2 week outcome in patients presenting with common physical complaints. Abstracts in *Clin Res* 41:579A, 1993; and *J Gen Intern Med* 9

- (suppl 2):96, 1994.
25. Komaroff AL, Buchwald D. Symptoms and signs of Chronic Fatigue Syndrome. *Rev Infect Dis* 1991;13(suppl 1):S8-S11.
 26. Buchwald D, Garrity D. Comparison of patients with Chronic Fatigue Syndrome, fibromyalgia, and multiple chemical sensitivities. *Arch Intern Med* 1994;154:2049-2053.
 27. Young MB, Mass AT, Alged JC. A controlled study of primary fibromyalgia syndrome: clinical features and association with other functional syndromes. *J Rheumatol* 1989;16(suppl 19):62-71.
 28. Mathew RJ, Weinman ML, Mirabi M. Physical symptoms of depression. *Br J Psychiatry* 1981;139:293-296.
 29. Hudson JI, Goldenberg DL, Pope HG, Keck PE, Schiesinger L. Comorbidity of fibromyalgia with medical and psychiatric disorders. *AM J Med* 1992;92:363-367.
 30. CDC, Unexplained Illness Among Persian Gulf War Veterans in an Air National Guard Unit: Preliminary Report - 1995. *MMWR* 1995;44:443-446.
 31. Schappert SM: National Ambulatory Medical Care Survey: 1989 summary. National Center for Health Statistics. *Vital Health Stat* 1992;13(110).
 32. Spitzer RL, Williams JBW, Kroenke K. Utility of a new procedure for diagnosing psychological conditions in primary care: The PRIME-MD 1000 study. *JAMA* 1994;272:1749-1756.
 33. Sartorius N, Goldberg D, de Girolamo G, Costa Silva JA, Lecrubier Y, Wittchen HU (eds). *Psychological Disorders in General Medical Settings*. Hogrefe & Huber: Toronto, 1990.
 34. American Psychiatric Association: *Diagnostic and Statistical Manual of Psychological Conditions*, Fourth Edition. Washington DC, American Psychiatric Association; 1994.
 35. Goldberg D, Huxley P. *Common Psychological Conditions: A Bio-Social Approach*. Routledge, New York, NY; 1992
 36. Cunningham LS, Kelsey, JL. Epidemiology of musculoskeletal impairments and associated disability. *Am J Public Health* 1984;74(6):574-9.
 37. McKee K, Gasser RA Jr, Magill AJ, Oster CN. *Diagnosis and Treatment of Diseases of Tactical Importance to US CENTCOM Forces 1990*. Washington DC: Office of the Surgeon General, U.S. Army, Oct 1990.
 38. Personal communication, Magill AJ, 2 June 95
 39. Price RK, North CS, Wessely S, Fraser VJ. Estimating the prevalence of chronic fatigue syndrome and associated symptoms in the community. *Pub Health Reports*. 1992; 107:514-22.
 40. Lloyd AR, Hickie I, Boughton CR, Spencer O, Wakefield D. Prevalence of fatigue syndrome in an Australian population. *Med Journ Australia*. 1990; 153:522-528.
 41. Wolfe F., Smythe HA, Yunus, MB, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. *Arthr Rheum*. 1990;33:160-172.
 42. Gallup Organization. *Sleep in America*. Princeton, NJ:Author. 1991.
 43. Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle aged adults. *N Engl J Med* 1993;328:1230-1235.
 44. Bresnitz EA, Goldberg R, Kosinski RM. Epidemiology of obstructive sleep apnea. *Epidemiologic Reviews*. 1994;16:210-227.
 45. Partinen M. *Principles and Practice of Sleep Medicine*. Philadelphia: W.B. Sanders, 1994.
 46. Morin CM. *Insomnia*. New York: Guilford Press, 1993;3-15.
 47. Lezak M. *Neuropsychological Assessment*. 2nd ed. New York: Oxford University Press, 1983.
 48. Miller WR. Psychological deficit in depression. *Psychological Bulletin* 1975;82:238-260.
 49. Kryger MH, Roth T, Dement W, eds, *Principles of sleep medicine*. Philadelphia: Sanders, 1989.
 50. Graffman J, Johnson, R Jr., Scheffers M Cognitive and mood-state changes in patients with chronic fatigue syndrome. *Reviews of Infection Diseases*. 1991;13(Suppl): 45-52
 51. U.S. Dept of Health & Human Services. Centers for Disease Control. *Field Epidemiology Report* 95-01. December 19, 1994.
 52. Final Report of Robbins AFB, GA Investigation. Armstrong Laboratory (AL/AOES) Brooks AFB, TX. (TVA-T03704,11-15 April 1994); June 21, 1994.
 53. Rosa C. Spontaneous abortion rate and the Gulf war mobilization. *J US Army Med Dept* Sep-Oct 1993;P8-8-93-9/10.
 54. Rubin HR, Gandek B, Rogers WH, Kosinski M, McHorney CA, Ware JE. Patients' ratings of outpatient visits in different practice settings: results from the Medical Outcomes Study. *JAMA* 1993;270:835-40.

55. Department of Veterans Affairs. Federal activities related to the health of Persian Gulf veterans. Department of Veterans Affairs, March 1995.
56. Lewis T. The Soldier's Heart and the Effort Syndrome. New York: Paul Hoeber (Ed), 1919:1-103.
57. DaCosta JM. On irritable heart: A clinical study of a form of functional cardiac disorder and its consequences. *Am J Med Sci* 1871;61:17-52.
58. Grinker RR, Spiegel JP. The Syndrome of "Operational Fatigue" (War Neuroses) in returnees. In: *Men Under Stress*, Maple Press Company, York, PA.
59. Bogen G. Symptoms in Vietnam Veterans Exposed To Agent Orange. *JAMA* 1979;242:2391.
60. Litz BT, Keane TM, Fisher L, Marx B, Monaco V. Physical health complaints in combat-related posttraumatic stress disorder: A preliminary report. *J Traumatic Stress* 1992; 5:131-141.
61. Baum A. Toxins, Technology and Natural Disasters. In Vandembos, G.R. & Bryant, B.K (Ed) *Cataclysms, Crises, and Catastrophes: Psychology in Action*. Washington, DC: American Psychological Association, 1987.
62. Fullerton C, Brandt G, Ursano R. Chemical and Biological Weapons: Silent Agents of Terror. In: *Emotional aftermath of the Persian Gulf War: Veterans, families, communities and Nations*. American Psychiatric Press, (in press/1996).
63. Pechura CM, Rall D.P.(Eds.): *Veterans at Risk: The Health Effects of Mustard Gas and Lewisite*. National Academy Press, Washington, D.C., 1993.